OIPE JG157
JUN 21 2001
PATENT & TRADEMARK OFFICE

Attorney's Docket No.: 07917-105001 / UMMC 00-04

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Craig C. Mello et al.
Serial No. : 09/689,992
Filed : October 13, 2000
Title : RNA INTERFERENCE PATHWAY GENES AS TOOLS FOR TARGETED GENETIC INTERFERENCE

Art Unit : 1656
Examiner : T. Strzelecka

BOX SEQUENCE
Commissioner for Patents
Washington, D.C. 20231

VERIFIED STATEMENT UNDER 37 CFR §1.821(f)

I, Maureen Ruttle, declare that I personally prepared the paper and the computer-readable copy of the Sequence Listing filed herewith for the above-identified application and that the content of both is the same.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of The United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: June 18, 2001

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Carla F. Fodile
Signature

CARLA F. O'Fodile
Typed or Printed Name of Person Signing Certificate

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SEQUENCE LISTING

<110> Mello, Craig C.
Tabara, Hiroaki
Grishok, Alla
Fire, Andrew

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Lys Thr Arg Gly Ile Arg Ser Lys Lys Lys Asp Ala Lys Asn Leu Ala
    210                 215                 220
Ala Trp Leu Met Trp Lys Ala Leu Glu Asp Gly Ile Glu Ser Leu Glu
225                 230                 235                 240
Ser Tyr Asp Met Val Asp Val Ile Glu Asn Leu Glu Glu Ala Glu His
                245                 250                 255
Leu Leu Glu Ile Gln Asp Gln Ala Ser Lys Ile Lys Asp Lys His Ser
            260                 265                 270
Ala Leu Ile Asp Ile Leu Ser Asp Lys Lys Arg Phe Ser Asp Tyr Ser
        275                 280                 285
Met Asp Phe Asn Val Leu Ser Val Ser Thr Met Gly Ile His Gln Val
    290                 295                 300
Leu Leu Glu Ile Ser Phe Arg Arg Leu Val Ser Pro Asp Pro Asp Asp
305                 310                 315                 320
Leu Glu Met Gly Ala Glu His Thr Gln Thr Glu Glu Ile Met Lys Ala
                325                 330                 335
Thr Ala Glu Lys Glu Lys Leu Arg Lys Lys Asn Met Pro Asp Ser Gly
            340                 345                 350
Pro Leu Val Phe Ala Gly His Gly Ser Ser Ala Glu Glu Ala Lys Gln
        355                 360                 365
Cys Ala Cys Lys Ser Ala Ile Ile His Phe Asn Thr Tyr Asp Phe Thr
    370                 375                 380
Asp Lys Tyr Tyr Cys Val Phe Leu Lys Asn Glu Ala Ser Glu Xaa Leu
385                 390                 395                 400
Xaa Lys Lys Lys Lys Lys
                405
```

<210> 6
<211> 763
<212> PRT
<213> Arabidopsis thaliana

<400> 6

```
Gly Ile Ile Asn Gly Pro Lys Arg Glu Arg Ser Tyr Lys Val Ala Ile
  1               5                  10                  15
Lys Phe Val Ala Arg Ala Asn Met His His Leu Gly Glu Phe Leu Ala
            20                  25                  30
Gly Lys Arg Ala Asp Cys Pro Gln Glu Ala Val Gln Ile Leu Asp Ile
        35                  40                  45
Val Leu Arg Glu Leu Ser Val Lys Arg Phe Cys Pro Val Gly Arg Ser
    50                  55                  60
```

```
Phe Phe Ser Pro Asp Ile Lys Thr Pro Gln Arg Leu Gly Glu Gly Leu
 65                  70                  75                  80
Glu Ser Trp Cys Gly Phe Tyr Gln Ser Ile Arg Pro Thr Gln Met Gly
                85                  90                  95
Leu Ser Leu Asn Ile Asp Met Ala Ser Ala Ala Phe Ile Glu Pro Leu
            100                 105                 110
Pro Val Ile Glu Phe Val Ala Gln Leu Leu Gly Lys Asp Val Leu Ser
        115                 120                 125
Lys Pro Leu Ser Asp Ser Asp Arg Val Lys Ile Lys Lys Gly Leu Arg
    130                 135                 140
Gly Val Lys Val Glu Val Thr His Arg Ala Asn Val Arg Arg Lys Tyr
145                 150                 155                 160
Arg Val Ala Gly Leu Thr Thr Gln Pro Thr Arg Glu Leu Met Phe Pro
                165                 170                 175
Val Asp Glu Asn Cys Thr Met Lys Ser Val Ile Glu Tyr Phe Gln Glu
            180                 185                 190
Met Tyr Gly Phe Thr Ile Gln His Thr His Leu Pro Cys Leu Gln Val
        195                 200                 205
Gly Asn Gln Lys Lys Ala Ser Tyr Leu Pro Met Glu Ala Cys Lys Ile
    210                 215                 220
Val Glu Gly Gln Arg Tyr Thr Lys Arg Leu Asn Glu Lys Gln Ile Thr
225                 230                 235                 240
Ala Leu Leu Lys Val Thr Cys Gln Arg Ala Glu Gly Gln Arg Asn Asp
                245                 250                 255
Ile Leu Arg Thr Val Gln His Asn Ala Tyr Asp Gln Asp Pro Tyr Ala
            260                 265                 270
Lys Glu Phe Gly Met Asn Ile Ser Glu Lys Leu Ala Ser Val Glu Ala
        275                 280                 285
Arg Ile Leu Pro Ala Pro Trp Leu Lys Tyr His Glu Asn Gly Lys Glu
    290                 295                 300
Lys Asp Cys Leu Pro Gln Val Gly Gln Trp Asn Met Met Asn Lys Lys
305                 310                 315                 320
Met Ile Asn Gly Met Thr Val Ser Arg Trp Ala Cys Val Asn Phe Ser
                325                 330                 335
Arg Ser Val Gln Glu Asn Val Ala Arg Gly Phe Cys Asn Glu Leu Gly
            340                 345                 350
Gln Met Cys Glu Val Ser Gly Met Glu Phe Asn Pro Glu Pro Val Ile
        355                 360                 365
Pro Ile Tyr Ser Ala Arg Pro Asp Gln Val Glu Lys Ala Leu Lys His
    370                 375                 380
Val Tyr His Thr Ser Met Asn Lys Thr Lys Gly Lys Glu Leu Glu Leu
385                 390                 395                 400
Leu Leu Ala Ile Leu Pro Asp Asn Asn Gly Ser Leu Tyr Gly Asp Leu
                405                 410                 415
Lys Arg Ile Cys Glu Thr Glu Leu Gly Leu Ile Ser Gln Cys Cys Leu
            420                 425                 430
Thr Lys His Val Phe Lys Ile Ser Lys Gln Tyr Leu Ala Asp Val Ser
        435                 440                 445
Leu Lys Ile Asn Val Lys Met Gly Gly Arg Asn Thr Val Leu Val Asp
    450                 455                 460
Ala Ile Ser Cys Arg Ile Pro Leu Val Ser Asp Ile Pro Thr Ile Ile
465                 470                 475                 480
Phe Gly Ala Asp Val Thr His Pro Glu Asn Gly Glu Glu Ser Ser Pro
                485                 490                 495
Ser Ile Ala Ala Val Val Ala Ser Gln Asp Trp Pro Glu Val Thr Lys
            500                 505                 510
```

```
Tyr Ala Gly Leu Val Cys Ala Gln Ala His Arg Gln Glu Leu Ile Gln
        515                 520                 525
Asp Leu Tyr Lys Thr Trp Gln Asp Pro Val Arg Gly Thr Val Ser Gly
    530                 535                 540
Gly Met Ile Arg Asp Leu Leu Ile Ser Phe Arg Lys Ala Thr Gly Gln
545                 550                 555                 560
Lys Pro Leu Arg Ile Ile Phe Tyr Arg Asp Gly Val Ser Glu Gly Gln
                565                 570                 575
Phe Tyr Gln Val Leu Leu Tyr Glu Leu Asp Ala Ile Arg Lys Ala Cys
            580                 585                 590
Ala Ser Leu Glu Pro Asn Tyr Gln Pro Pro Val Thr Phe Ile Val Val
        595                 600                 605
Gln Lys Arg His His Thr Arg Leu Phe Ala Asn Asn His Arg Asp Lys
    610                 615                 620
Asn Ser Thr Asp Arg Ser Gly Asn Ile Leu Pro Gly Thr Val Val Asp
625                 630                 635                 640
Thr Lys Ile Cys His Pro Thr Glu Phe Asp Phe Tyr Leu Cys Ser His
                645                 650                 655
Ala Gly Ile Gln Gly Thr Ser Arg Pro Ala His Tyr His Val Leu Trp
            660                 665                 670
Asp Glu Asn Asn Phe Thr Ala Asp Gly Ile Gln Ser Leu Thr Asn Asn
        675                 680                 685
Leu Cys Tyr Thr Tyr Ala Arg Cys Thr Arg Ser Val Ser Ile Val Pro
    690                 695                 700
Pro Ala Tyr Tyr Ala His Leu Ala Ala Phe Arg Ala Arg Phe Tyr Leu
705                 710                 715                 720
Glu Pro Glu Ile Met Gln Asp Asn Gly Ser Pro Gly Lys Lys Asn Thr
                725                 730                 735
Lys Thr Thr Thr Val Gly Asp Val Gly Val Lys Pro Leu Pro Ala Leu
            740                 745                 750
Lys Glu Asn Val Lys Arg Val Met Phe Tyr Cys
        755                 760
```

<210> 7
<211> 678
<212> PRT
<213> Drosophila melanogaster

<400> 7

```
Arg Ala Gly Glu Asn Ile Glu Ile Lys Ile Lys Ala Val Gly Ser Val
  1               5                  10                  15
Gln Ser Thr Asp Ala Glu Gln Phe Gln Val Leu Asn Leu Ile Leu Arg
            20                  25                  30
Arg Ala Met Glu Gly Leu Asp Leu Lys Leu Val Ser Arg Tyr Tyr Tyr
        35                  40                  45
Asp Pro Gln Ala Lys Ile Asn Leu Glu Asn Phe Arg Met Gln Leu Trp
    50                  55                  60
Pro Gly Tyr Gln Thr Ser Ile Arg Gln His Glu Asn Asp Ile Leu Leu
65                  70                  75                  80
Cys Ser Glu Ile Cys His Lys Val Met Arg Thr Glu Thr Leu Tyr Asn
                85                  90                  95
Ile Leu Ser Asp Ala Ile Arg Asp Ser Asp Asp Tyr Gln Ser Thr Phe
            100                 105                 110
Lys Arg Ala Val Met Gly Met Val Ile Leu Thr Asp Tyr Asn Asn Lys
        115                 120                 125
Thr Tyr Arg Ile Asp Asp Val Asp Phe Gln Ser Thr Pro Leu Cys Lys
    130                 135                 140
```

```
Phe Lys Thr Asn Asp Gly Glu Ile Ser Tyr Val Asp Tyr Tyr Lys Lys
145                 150                 155                 160
Arg Tyr Asn Ile Ile Ile Arg Asp Leu Lys Gln Pro Leu Val Met Ser
                165                 170                 175
Arg Pro Thr Asp Lys Asn Ile Arg Gly Gly Asn Asp Gln Ala Ile Met
            180                 185                 190
Ile Ile Pro Glu Leu Ala Arg Ala Thr Gly Met Thr Asp Ala Met Arg
        195                 200                 205
Ala Asp Phe Arg Thr Leu Arg Ala Met Ser Glu His Thr Arg Leu Asn
    210                 215                 220
Pro Asp Arg Arg Ile Glu Arg Leu Arg Met Phe Asn Lys Arg Leu Lys
225                 230                 235                 240
Ser Cys Lys Gln Ser Val Glu Thr Leu Lys Ser Trp Asn Ile Glu Leu
                245                 250                 255
Asp Ser Ala Leu Val Glu Ile Pro Ala Arg Val Leu Pro Pro Glu Lys
            260                 265                 270
Ile Leu Phe Gly Asn Gln Lys Ile Phe Val Cys Asp Ala Arg Ala Asp
        275                 280                 285
Trp Thr Asn Glu Phe Arg Thr Cys Ser Met Phe Lys Asn Val His Ile
    290                 295                 300
Asn Arg Trp Tyr Val Ile Thr Pro Ser Arg Asn Leu Arg Glu Thr Gln
305                 310                 315                 320
Glu Phe Val Gln Met Cys Ile Arg Thr Ala Ser Ser Met Lys Met Asn
                325                 330                 335
Ile Cys Asn Pro Ile Tyr Glu Glu Ile Pro Asp Asp Arg Asn Gly Thr
            340                 345                 350
Tyr Ser Gln Ala Ile Asp Asn Ala Ala Ala Asn Asp Pro Gln Ile Val
        355                 360                 365
Met Val Val Met Arg Ser Pro Asn Glu Glu Lys Tyr Ser Cys Ile Lys
    370                 375                 380
Lys Arg Thr Cys Val Asp Arg Pro Val Pro Ser Gln Val Val Thr Leu
385                 390                 395                 400
Lys Val Ile Ala Pro Arg Gln Gln Lys Pro Thr Gly Leu Met Ser Ile
                405                 410                 415
Ala Thr Lys Val Val Ile Gln Met Asn Ala Lys Leu Met Gly Ala Pro
            420                 425                 430
Trp Gln Val Val Ile Pro Leu His Gly Leu Met Thr Val Gly Phe Asp
        435                 440                 445
Val Cys His Ser Pro Lys Asn Lys Asn Lys Ser Tyr Gly Ala Phe Val
    450                 455                 460
Ala Thr Met Asp Gln Lys Glu Ser Phe Arg Tyr Phe Ser Thr Val Asn
465                 470                 475                 480
Glu His Ile Lys Gly Gln Glu Leu Ser Glu Gln Met Ser Val Asn Met
                485                 490                 495
Ala Cys Ala Leu Arg Ser Tyr Gln Glu Gln His Arg Ser Leu Pro Glu
            500                 505                 510
Arg Ile Leu Phe Phe Arg Asp Gly Val Gly Asp Gly Gln Leu Tyr Gln
        515                 520                 525
Val Val Asn Ser Glu Val Asn Thr Leu Lys Asp Arg Leu Asp Glu Ile
    530                 535                 540
Tyr Lys Ser Ala Gly Lys Gln Glu Gly Cys Arg Met Thr Phe Ile Ile
545                 550                 555                 560
Val Ser Lys Arg Ile Asn Ser Arg Tyr Phe Thr Gly His Arg Asn Pro
                565                 570                 575
Val Pro Gly Thr Val Val Asp Asp Val Ile Thr Leu Pro Glu Arg Tyr
            580                 585                 590
```

```
Asp Phe Phe Leu Val Ser Gln Ala Val Arg Ile Gly Thr Val Ser Pro
        595                 600                 605
Thr Ser Tyr Asn Val Ile Ser Asp Asn Met Gly Leu Asn Ala Asp Lys
    610                 615                 620
Leu Gln Met Leu Ser Tyr Lys Met Thr His Met Tyr Tyr Asn Tyr Ser
625                 630                 635                 640
Gly Thr Ile Arg Val Pro Ala Val Cys His Tyr Ala His Lys Leu Ala
                645                 650                 655
Phe Leu Val Ala Glu Ser Ile Asn Arg Ala Pro Ser Ala Gly Leu Gln
            660                 665                 670
Asn Gln Leu Tyr Phe Leu
        675
```

<210> 8
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Consensus sequence

<400> 8

```
Pro Leu Glu Gln Tyr Gly Pro His Phe Val Gly Gly Gly Ser Lys Lys
  1               5                  10                  15
Ala Lys Ala Ala Ala Leu Leu
            20
```

<210> 9
<211> 766
<212> PRT
<213> Caenorhabditis elegans

<400> 9

```
Ser Ala Val Glu Arg Gln Phe Ser Val Ser Leu Lys Trp Val Gly Gln
  1               5                  10                  15
Val Ser Leu Ser Thr Leu Glu Asp Ala Met Glu Gly Arg Val Arg Gln
            20                  25                  30
Val Pro Phe Glu Ala Val Gln Ala Met Asp Val Ile Leu Arg His Leu
        35                  40                  45
Pro Ser Leu Lys Tyr Thr Pro Val Gly Arg Ser Phe Phe Ser Pro Pro
    50                  55                  60
Val Pro Asn Ala Ser Gly Val Met Ala Gly Ser Cys Pro Pro Gln Ala
65                  70                  75                  80
Ser Gly Ala Val Ala Gly Gly Ala His Ser Ala Gly Gln Tyr His Ala
                85                  90                  95
Glu Ser Lys Leu Gly Gly Gly Arg Glu Val Trp Phe Gly Phe His Gln
            100                 105                 110
Ser Val Arg Pro Ser Gln Trp Lys Met Met Leu Asn Ile Asp Val Ser
        115                 120                 125
Ala Thr Ala Phe Tyr Arg Ser Met Pro Val Ile Glu Phe Ile Ala Glu
    130                 135                 140
Val Leu Glu Leu Pro Val Gln Ala Leu Ala Glu Arg Arg Ala Leu Ser
145                 150                 155                 160
Asp Ala Gln Arg Val Lys Phe Thr Lys Glu Ile Arg Gly Leu Lys Ile
                165                 170                 175
Glu Ile Thr His Cys Gly Gln Met Arg Arg Lys Tyr Arg Val Cys Asn
            180                 185                 190
```

```
Val Thr Arg Arg Pro Ala Gln Thr Gln Thr Phe Pro Leu Gln Leu Glu
        195                 200                 205
Thr Gly Gln Thr Ile Glu Cys Thr Val Ala Lys Tyr Phe Tyr Asp Lys
    210                 215                 220
Tyr Arg Ile Gln Leu Lys Tyr Pro His Leu Pro Cys Leu Gln Val Gly
225                 230                 235                 240
Gln Glu Gln Lys His Thr Tyr Leu Pro Pro Glu Val Cys Asn Ile Val
                245                 250                 255
Pro Gly Gln Arg Cys Ile Lys Lys Leu Thr Asp Val Gln Thr Ser Thr
            260                 265                 270
Met Ile Lys Ala Thr Ala Arg Ser Ala Pro Glu Arg Glu Arg Glu Ile
        275                 280                 285
Ser Asn Leu Val Arg Lys Ala Glu Phe Ser Ala Asp Pro Phe Ala His
    290                 295                 300
Glu Phe Gly Ile Thr Ile Asn Pro Ala Met Thr Glu Val Lys Gly Arg
305                 310                 315                 320
Val Leu Ser Ala Pro Lys Leu Leu Tyr Gly Gly Arg Thr Arg Ala Thr
                325                 330                 335
Ala Leu Pro Asn Gln Gly Val Trp Asp Met Arg Gly Lys Gln Phe His
            340                 345                 350
Thr Gly Ile Asp Val Arg Val Trp Ala Ile Ala Cys Phe Ala Gln Gln
        355                 360                 365
Gln His Val Lys Glu Asn Asp Leu Arg Met Phe Thr Asn Gln Leu Gln
    370                 375                 380
Arg Ile Ser Asn Asp Ala Gly Met Pro Ile Val Gly Asn Pro Cys Phe
385                 390                 395                 400
Cys Lys Tyr Ala Val Gly Val Glu Gln Val Glu Pro Met Phe Lys Tyr
                405                 410                 415
Leu Lys Gln Asn Tyr Ser Gly Ile Gln Leu Val Val Val Val Leu Pro
            420                 425                 430
Gly Lys Thr Pro Val Tyr Ala Glu Val Lys Arg Val Gly Asp Thr Val
        435                 440                 445
Leu Gly Ile Ala Thr Gln Cys Val Gln Ala Lys Asn Ala Ile Arg Thr
    450                 455                 460
Thr Pro Gln Thr Leu Ser Asn Leu Cys Leu Lys Met Asn Val Lys Leu
465                 470                 475                 480
Gly Gly Val Asn Ser Ile Leu Leu Pro Asn Val Arg Pro Arg Ile Phe
                485                 490                 495
Asn Glu Pro Val Ile Phe Phe Gly Cys Asp Ile Thr His Pro Pro Ala
            500                 505                 510
Gly Asp Ser Arg Lys Pro Ser Ile Ala Ala Val Val Gly Ser Met Asp
        515                 520                 525
Ala His Pro Ser Arg Tyr Ala Ala Thr Val Arg Val Gln Gln His Arg
    530                 535                 540
Gln Glu Ile Ile Ser Asp Leu Thr Tyr Met Val Arg Glu Leu Leu Val
545                 550                 555                 560
Gln Phe Tyr Arg Asn Thr Arg Phe Lys Pro Ala Arg Ile Val Val Tyr
                565                 570                 575
Arg Asp Gly Val Ser Glu Gly Gln Phe Phe Asn Val Leu Gln Tyr Glu
            580                 585                 590
Leu Arg Ala Ile Arg Glu Ala Cys Met Met Leu Glu Arg Gly Tyr Gln
        595                 600                 605
Pro Gly Ile Thr Phe Ile Ala Val Gln Lys Arg His His Thr Arg Leu
    610                 615                 620
Phe Ala Val Asp Lys Lys Asp Gln Val Gly Lys Ala Tyr Asn Ile Pro
625                 630                 635                 640
```

```
Pro Gly Thr Thr Val Asp Val Gly Ile Thr His Pro Thr Glu Phe Asp
                645                 650                 655
Phe Tyr Leu Cys Ser His Ala Gly Ile Gln Gly Thr Ser Arg Pro Ser
            660                 665                 670
His Tyr His Val Leu Trp Asp Asp Asn Asn Leu Thr Ala Asp Glu Leu
        675                 680                 685
Gln Gln Leu Thr Tyr Gln Met Cys His Thr Tyr Val Arg Cys Thr Arg
    690                 695                 700
Ser Val Ser Ile Pro Ala Pro Ala Tyr Tyr Ala His Leu Val Ala Phe
705                 710                 715                 720
Arg Ala Arg Tyr His Leu Val Asp Arg Glu His Asp Ser Gly Glu Gly
                725                 730                 735
Ser Gln Pro Ser Gly Thr Ser Glu Asp Thr Thr Leu Ser Asn Met Ala
            740                 745                 750
Arg Ala Val Gln Val Ile Leu Ala Phe Asn Leu Val Ser Ile
        755                 760                 765
```

<210> 10
<211> 737
<212> PRT
<213> Oryctolagus cuniculus

<400> 10

```
Gly Lys Asp Arg Ile Phe Lys Val Ser Ile Lys Trp Val Ser Cys Val
  1               5                  10                  15
Ser Leu Gln Ala Leu His Asp Ala Leu Ser Gly Arg Leu Pro Ser Val
            20                  25                  30
Pro Phe Glu Thr Ile Gln Ala Leu Asp Val Val Met Arg His Leu Pro
        35                  40                  45
Ser Met Arg Tyr Thr Pro Val Gly Arg Ser Phe Phe Thr Ala Ser Glu
    50                  55                  60
Gly Cys Ser Asn Pro Leu Gly Gly Gly Arg Glu Val Trp Phe Gly Phe
65                  70                  75                  80
His Gln Ser Val Arg Pro Ser Leu Trp Lys Met Met Leu Asn Ile Asp
                85                  90                  95
Val Ser Ala Thr Ala Phe Tyr Lys Ala Gln Pro Val Ile Glu Phe Val
            100                 105                 110
Cys Glu Val Leu Asp Phe Lys Ser Ile Glu Glu Gln Gln Lys Pro Leu
        115                 120                 125
Thr Asp Ser Gln Arg Val Lys Phe Thr Lys Glu Ile Lys Gly Leu Lys
    130                 135                 140
Val Glu Ile Thr His Cys Gly Gln Met Lys Arg Lys Tyr Arg Val Cys
145                 150                 155                 160
Asn Val Thr Arg Arg Pro Ala Ser His Gln Thr Phe Pro Leu Gln Gln
                165                 170                 175
Glu Ser Gly Gln Thr Val Glu Cys Thr Val Ala Gln Tyr Phe Lys Asp
            180                 185                 190
Arg His Lys Leu Val Leu Arg Tyr Pro His Leu Pro Cys Leu Gln Val
        195                 200                 205
Gly Gln Glu Gln Lys His Thr Tyr Leu Pro Leu Glu Val Cys Asn Ile
    210                 215                 220
Val Ala Gly Gln Arg Cys Ile Lys Lys Leu Thr Asp Asn Gln Thr Ser
225                 230                 235                 240
Thr Met Ile Arg Ala Thr Ala Arg Ser Ala Pro Asp Arg Gln Glu Glu
                245                 250                 255
Ile Ser Lys Leu Met Arg Ser Ala Ser Phe Asn Thr Asp Pro Tyr Val
            260                 265                 270
```

```
Arg Glu Phe Gly Ile Met Val Lys Asp Glu Met Thr Asp Val Thr Gly
        275                 280                 285
Arg Val Leu Gln Pro Pro Ser Ile Leu Tyr Gly Gly Arg Asn Lys Ala
    290                 295                 300
Ile Ala Thr Pro Val Gln Gly Val Trp Asp Met Arg Asn Lys Gln Phe
305                 310                 315                 320
His Thr Gly Ile Glu Ile Lys Val Trp Ala Ile Ala Cys Phe Ala Pro
                325                 330                 335
Gln Arg Gln Cys Thr Glu Val His Leu Lys Ser Phe Thr Glu Gln Leu
            340                 345                 350
Arg Lys Ile Ser Arg Asp Ala Gly Met Pro Ile Gln Gly Gln Pro Cys
        355                 360                 365
Phe Cys Lys Tyr Ala Gln Gly Ala Asp Ser Val Gly Pro Met Phe Arg
    370                 375                 380
His Leu Lys Asn Thr Tyr Ala Gly Leu Gln Leu Val Val Val Ile Leu
385                 390                 395                 400
Pro Gly Lys Thr Pro Val Tyr Ala Glu Val Lys Arg Val Gly Asp Thr
                405                 410                 415
Val Leu Gly Met Ala Thr Gln Cys Val Gln Met Lys Asn Val Gln Arg
            420                 425                 430
Thr Thr Pro Gln Thr Leu Ser Asn Leu Cys Leu Lys Ile Asn Val Lys
        435                 440                 445
Leu Gly Gly Val Asn Asn Ile Leu Leu Pro Gln Gly Arg Pro Pro Val
    450                 455                 460
Phe Gln Gln Pro Val Ile Phe Leu Gly Ala Asp Val Thr His Pro Pro
465                 470                 475                 480
Ala Gly Asp Gly Lys Lys Pro Ser Ile Ala Ala Val Val Gly Ser Met
                485                 490                 495
Asp Ala His Pro Asn Arg Tyr Cys Ala Thr Val Arg Val Gln Gln His
            500                 505                 510
Arg Gln Glu Ile Ile Gln Asp Leu Ala Ala Met Val Arg Glu Leu Leu
        515                 520                 525
Ile Gln Phe Tyr Lys Ser Thr Arg Phe Lys Pro Thr Arg Ile Ile Phe
    530                 535                 540
Tyr Arg Asp Gly Val Ser Glu Gly Gln Phe Gln Gln Val Leu His His
545                 550                 555                 560
Glu Leu Leu Ala Ile Arg Glu Ala Cys Ile Lys Leu Glu Lys Asp Tyr
                565                 570                 575
Gln Pro Gly Ile Thr Phe Ile Val Val Gln Lys Arg His His Thr Arg
            580                 585                 590
Leu Phe Cys Thr Asp Lys Asn Glu Arg Val Gly Lys Ser Gly Asn Ile
        595                 600                 605
Pro Ala Gly Thr Thr Val Asp Thr Lys Ile Thr His Pro Thr Glu Phe
    610                 615                 620
Asp Phe Tyr Leu Cys Ser His Ala Gly Ile Gln Gly Thr Ser Arg Pro
625                 630                 635                 640
Ser His Tyr His Val Leu Trp Asp Asp Asn Arg Phe Ser Ser Asp Glu
                645                 650                 655
Leu Gln Ile Leu Thr Tyr Gln Leu Cys His Thr Tyr Val Arg Cys Thr
            660                 665                 670
Arg Ser Val Ser Ile Pro Ala Pro Ala Tyr Tyr Ala His Leu Val Ala
        675                 680                 685
Phe Arg Ala Arg Tyr His Leu Val Asp Lys Glu His Asp Ser Ala Glu
    690                 695                 700
Gly Ser His Thr Ser Gly Gln Ser Asn Gly Arg Asp His Gln Ala Leu
705                 710                 715                 720
```

Ala Lys Ala Val Gln Val His Gln Asp Thr Leu Arg Thr Met Tyr Phe
725 730 735
Ala

<210> 11
<211> 298
<212> PRT
<213> Xenopus laevis

<400> 11
Met Ser Ser Glu Lys Pro Thr Ser Leu Asn Ala Met Arg Ala Thr Asn
1 5 10 15
Pro Cys Glu Thr Pro Ile Gln Leu Leu His Glu Phe Gly Thr Lys Thr
20 25 30
Gly Asn His Pro Val Tyr Thr Leu Glu Lys Ala Glu Gly Gln Ala His
35 40 45
Asn Pro Ser Phe Thr Phe Arg Leu Val Ile Gly Asp Ile Thr Ser Leu
50 55 60
Gly Glu Gly Pro Ser Lys Lys Thr Pro Lys Gln Lys Ala Ala Glu Phe
65 70 75 80
Ala Leu Asn Ile Leu Arg Gly Asp Thr Ser Lys Cys Leu Pro Val Thr
85 90 95
Asp Thr Leu Arg Asp Pro Lys Lys Pro Pro Asn Gln Met Gln Glu Asn
100 105 110
Pro Val Gly Ser Leu Gln Glu Leu Ala Val Gln Lys Gly Trp Arg Leu
115 120 125
Pro Glu Tyr Thr Val Ala Gln Glu Ser Gly Pro Pro His Lys Arg Glu
130 135 140
Phe Thr Ile Thr Cys Arg Val Glu Thr Phe Val Glu Thr Gly Ser Gly
145 150 155 160
Thr Ser Lys Gln Val Ala Lys Arg Val Ala Ala Glu Lys Leu Leu Thr
165 170 175
Lys Phe Lys Thr Ile Ser Thr Asp Asn Ile Pro Leu Asn Lys Leu Ile
180 185 190
Gly Asn Lys Met Gly Cys Thr Trp Asp Ser Met Arg Asn Ser Ser Gly
195 200 205
Glu Lys Ile Ser Met Leu Lys Arg Ser Pro Leu Ser Ile Pro Asn Thr
210 215 220
Asp Tyr Val Lys Met Leu Lys Asp Val Ala Glu Glu Leu Asp Phe Asn
225 230 235 240
Leu Thr Tyr Leu Asp Ile Asp Glu Leu Ser Val Asn Gly Gln Tyr Gln
245 250 255
Cys Leu Ala Glu Leu Ser Thr Asn Pro Ile Thr Val Cys His Gly Thr
260 265 270
Gly Ile Ser Cys Gly Asn Ala His Asn Asp Ala Ala His Asn Ala Leu
275 280 285
Gln Tyr Leu Lys Ile Met Cys Ile Lys Lys
290 295

<210> 12
<211> 551
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT

<222> (1)...(551)
<223> Xaa = Any Amino Acid

<400> 12

```
Met Ala Gly Asp Leu Ser Ala Gly Phe Phe Met Glu Glu Leu Asn Thr
  1               5                  10                  15
Tyr Arg Gln Lys Gln Gly Val Val Leu Lys Tyr Gln Glu Leu Pro Asn
             20                  25                  30
Ser Gly Pro Pro His Asp Arg Arg Phe Thr Phe Gln Val Ile Ile Asp
         35                  40                  45
Gly Arg Glu Phe Pro Glu Gly Glu Gly Arg Ser Lys Lys Glu Ala Xaa
     50                  55                  60
Asn Ala Ala Ala Xaa Leu Ala Val Glu Ile Leu Asn Lys Glu Lys Lys
 65                  70                  75                  80
Ala Val Ser Pro Leu Leu Leu Thr Thr Thr Asn Ser Ser Glu Gly Leu
                 85                  90                  95
Ser Met Gly Asn Tyr Ile Gly Leu Ile Asn Arg Ile Ala Gln Lys Lys
            100                 105                 110
Arg Leu Thr Val Asn Tyr Glu Gln Cys Ala Ser Gly Val His Gly Pro
        115                 120                 125
Glu Gly Phe His Tyr Lys Cys Lys Met Gly Gln Lys Glu Tyr Ser Ile
    130                 135                 140
Gly Thr Gly Ser Thr Lys Gln Glu Ala Lys Gln Leu Ala Ala Lys Leu
145                 150                 155                 160
Ala Tyr Leu Gln Ile Leu Ser Glu Glu Thr Ser Val Lys Ser Asp Tyr
                165                 170                 175
Leu Ser Ser Gly Ser Phe Ala Thr Thr Cys Glu Ser Gln Ser Asn Ser
            180                 185                 190
Leu Val Thr Ser Thr Leu Ala Ser Glu Ser Ser Ser Glu Gly Asp Phe
        195                 200                 205
Ser Ala Asp Thr Ser Glu Ile Asn Ser Asn Ser Asp Ser Leu Asn Ser
    210                 215                 220
Ser Ser Leu Leu Met Asn Gly Leu Arg Asn Asn Gln Arg Lys Ala Lys
225                 230                 235                 240
Arg Ser Leu Ala Pro Arg Phe Asp Leu Pro Asp Met Lys Glu Thr Lys
                245                 250                 255
Tyr Thr Val Asp Lys Arg Phe Gly Met Asp Phe Lys Glu Ile Glu Leu
            260                 265                 270
Ile Gly Ser Gly Gly Phe Gly Gln Val Phe Lys Ala Lys His Arg Ile
        275                 280                 285
Asp Gly Lys Thr Tyr Val Ile Lys Arg Val Lys Tyr Asn Asn Glu Lys
    290                 295                 300
Ala Glu Arg Glu Val Lys Ala Leu Ala Lys Leu Asp His Val Asn Ile
305                 310                 315                 320
Val His Tyr Asn Gly Cys Trp Asp Gly Phe Asp Tyr Asp Pro Glu Thr
                325                 330                 335
Ser Asp Asp Ser Leu Glu Ser Ser Asp Tyr Asp Pro Glu Asn Ser Lys
            340                 345                 350
Asn Ser Ser Arg Ser Lys Thr Lys Cys Leu Phe Ile Gln Met Glu Phe
        355                 360                 365
Cys Asp Lys Gly Thr Leu Glu Gln Trp Ile Glu Lys Arg Arg Gly Glu
    370                 375                 380
Lys Leu Asp Lys Val Leu Ala Leu Glu Leu Phe Glu Gln Ile Thr Lys
385                 390                 395                 400
Gly Val Asp Tyr Ile His Ser Lys Lys Leu Ile His Arg Asp Leu Lys
                405                 410                 415
```

```
Pro Ser Asn Ile Phe Leu Val Asp Thr Lys Gln Val Lys Ile Gly Asp
            420                 425                 430
Phe Gly Leu Val Thr Ser Leu Lys Asn Asp Gly Lys Arg Thr Arg Ser
        435                 440                 445
Lys Gly Thr Leu Arg Tyr Met Ser Pro Glu Gln Ile Ser Ser Gln Asp
    450                 455                 460
Tyr Gly Lys Glu Val Asp Leu Tyr Ala Leu Gly Leu Ile Leu Ala Glu
465                 470                 475                 480
Leu Leu His Val Cys Asp Thr Ala Phe Glu Thr Ser Lys Phe Phe Thr
                485                 490                 495
Asp Leu Arg Asp Gly Ile Ile Ser Asp Ile Xaa Asp Lys Lys Glu Glu
            500                 505                 510
Thr Leu Leu Gln Lys Leu Leu Ser Lys Xaa Pro Glu Asp Arg Pro Asn
        515                 520                 525
Thr Ser Glu Ile Leu Arg Thr Leu Thr Val Trp Lys Lys Ser Pro Glu
    530                 535                 540
Lys Asn Glu Arg His Thr Cys
545                 550
```

<210> 13
<211> 818
<212> PRT
<213> Caenorhabditis elegans

<400> 13

```
Val Asn Glu Glu Ile Lys Val Gln Phe Ala Lys Asn Phe Val Tyr Asp
  1               5                  10                  15
Asn Asn Ser Ile Leu Arg Val Pro Glu Ser Phe His Asp Pro Asn Arg
            20                  25                  30
Phe Glu Gln Ser Leu Glu Val Ala Pro Arg Ile Glu Ala Trp Phe Gly
        35                  40                  45
Ile Tyr Ile Gly Ile Lys Glu Leu Phe Asp Gly Glu Pro Val Leu Asn
    50                  55                  60
Phe Ala Ile Val Asp Lys Leu Phe Tyr Asn Ala Pro Lys Met Ser Leu
65                  70                  75                  80
Leu Asp Tyr Leu Leu Leu Ile Val Asp Pro Gln Ser Cys Asn Asp Asp
                85                  90                  95
Val Arg Lys Asp Leu Lys Thr Lys Leu Met Ala Gly Lys Met Thr Ile
            100                 105                 110
Arg Gln Ala Ala Arg Pro Arg Ile Arg Gln Leu Leu Glu Asn Leu Lys
        115                 120                 125
Leu Lys Cys Ala Glu Val Trp Asp Asn Glu Met Ser Arg Leu Thr Glu
    130                 135                 140
Arg His Leu Thr Phe Leu Asp Leu Cys Glu Glu Asn Ser Leu Val Tyr
145                 150                 155                 160
Lys Val Thr Gly Lys Ser Asp Arg Gly Arg Asn Ala Lys Lys Tyr Asp
                165                 170                 175
Thr Thr Leu Phe Lys Ile Tyr Glu Glu Asn Lys Lys Phe Ile Glu Phe
            180                 185                 190
Pro His Leu Pro Leu Val Lys Val Lys Ser Gly Ala Lys Glu Tyr Ala
        195                 200                 205
Val Pro Met Glu His Leu Glu Val His Glu Lys Pro Gln Arg Tyr Lys
    210                 215                 220
Asn Arg Ile Asp Leu Val Met Gln Asp Lys Phe Leu Lys Arg Ala Thr
225                 230                 235                 240
Arg Lys Pro His Asp Tyr Lys Glu Asn Thr Leu Lys Met Leu Lys Glu
                245                 250                 255
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Leu Asp Phe Ser Ser Glu Glu Leu Asn Phe Val Glu Arg Phe Gly Leu
            260                 265                 270
Cys Ser Lys Leu Gln Met Ile Glu Cys Pro Gly Lys Val Leu Lys Glu
        275                 280                 285
Pro Met Leu Val Asn Ser Val Asn Glu Gln Ile Lys Met Thr Pro Val
    290                 295                 300
Ile Arg Gly Phe Gln Glu Lys Gln Leu Asn Val Val Pro Glu Lys Glu
305                 310                 315                 320
Leu Cys Cys Ala Val Phe Val Val Asn Glu Thr Ala Gly Asn Pro Cys
                325                 330                 335
Leu Glu Glu Asn Asp Val Val Lys Phe Tyr Thr Glu Leu Ile Gly Gly
            340                 345                 350
Cys Lys Phe Arg Gly Ile Arg Ile Gly Ala Asn Glu Asn Arg Gly Ala
        355                 360                 365
Gln Ser Ile Met Tyr Asp Ala Thr Lys Asn Glu Tyr Ala Phe Tyr Lys
    370                 375                 380
Asn Cys Thr Leu Asn Thr Gly Ile Gly Arg Phe Glu Ile Ala Ala Thr
385                 390                 395                 400
Glu Ala Lys Asn Met Phe Glu Arg Leu Pro Asp Lys Glu Gln Lys Val
                405                 410                 415
Leu Met Phe Ile Ile Ile Ser Lys Arg Gln Leu Asn Ala Tyr Gly Phe
            420                 425                 430
Val Lys His Tyr Cys Asp His Thr Ile Gly Val Ala Asn Gln His Ile
        435                 440                 445
Thr Ser Glu Thr Val Thr Lys Ala Leu Ala Ser Leu Arg His Glu Lys
    450                 455                 460
Gly Ser Lys Arg Ile Phe Tyr Gln Ile Ala Leu Lys Ile Asn Ala Lys
465                 470                 475                 480
Leu Gly Gly Ile Asn Gln Glu Leu Asp Trp Ser Glu Ile Ala Glu Ile
                485                 490                 495
Ser Pro Glu Glu Lys Glu Arg Arg Lys Thr Met Pro Leu Thr Met Tyr
            500                 505                 510
Val Gly Ile Asp Val Thr His Pro Thr Ser Tyr Ser Gly Ile Asp Tyr
        515                 520                 525
Ser Ile Ala Ala Val Val Ala Ser Ile Asn Pro Gly Gly Thr Ile Tyr
    530                 535                 540
Arg Asn Met Ile Val Thr Gln Glu Glu Cys Arg Pro Gly Glu Arg Ala
545                 550                 555                 560
Val Ala His Gly Arg Glu Arg Thr Asp Ile Leu Glu Ala Lys Phe Val
                565                 570                 575
Lys Leu Leu Arg Glu Phe Ala Glu Asn Asn Asp Asn Arg Ala Pro Ala
            580                 585                 590
His Ile Val Val Tyr Arg Asp Gly Val Ser Asp Ser Glu Met Leu Arg
        595                 600                 605
Val Ser His Asp Glu Leu Arg Ser Leu Lys Ser Glu Val Lys Gln Phe
    610                 615                 620
Met Ser Glu Arg Asp Gly Glu Asp Pro Glu Pro Lys Tyr Thr Phe Ile
625                 630                 635                 640
Val Ile Gln Lys Arg His Asn Thr Arg Leu Leu Arg Arg Met Glu Lys
                645                 650                 655
Asp Lys Pro Val Val Asn Lys Asp Leu Thr Pro Ala Glu Thr Asp Val
            660                 665                 670
Ala Val Ala Ala Val Lys Gln Trp Glu Glu Asp Met Lys Glu Ser Lys
        675                 680                 685
Glu Thr Gly Ile Val Asn Pro Ser Ser Gly Thr Thr Val Asp Lys Leu
    690                 695                 700
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Ile Val Ser Lys Tyr Lys Phe Asp Phe Phe Leu Ala Ser His His Gly
705 710 715 720
Val Leu Gly Thr Ser Arg Pro Gly His Tyr Thr Val Met Tyr Asp Asp
725 730 735
Lys Gly Met Ser Gln Asp Glu Val Tyr Lys Met Thr Tyr Gly Leu Ala
740 745 750
Phe Leu Ser Ala Arg Cys Arg Lys Pro Ile Ser Leu Pro Val Pro Val
755 760 765
His Tyr Ala His Leu Ser Cys Glu Lys Ala Lys Glu Leu Tyr Arg Thr
770 775 780
Tyr Lys Glu His Tyr Ile Gly Asp Tyr Ala Gln Pro Arg Thr Arg His
785 790 795 800
Glu Met Glu His Phe Leu Gln Thr Asn Val Lys Tyr Pro Gly Met Ser
805 810 815
Phe Ala

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<211> 63
<212> PRT
<213> Caenorhabditis elegans

<400> 14
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Ile Cys Thr Met Cys Asn Gln Lys Thr Arg Gly Ile Thr Ser Lys Gln
35 40 45
Lys Asp Ala Lys Asn Leu Ala Ala Trp Leu Met Trp Lys Ala Leu
50 55 60

a4 cont

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<211> 9
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<213> Artificial Sequence

<220>
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<400> 15
Gln Glu Tyr His Phe Ser Lys Gln Lys
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